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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/659,782	09/11/2003	Liat Mintz	28238	6045

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POTTER ANDERSON & CORROON LLP
ATTN: KATHLEEN W. GEIGER, ESQ.
P.O. BOX 951
WILMINGTON, DE 19899-0951

EXAMINER	
DUNSTON, JENNIFER ANN	
ART UNIT	**PAPER NUMBER**
1636	

DATE MAILED: 08/25/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/659,782	MINTZ, LIAT	
	Examiner	Art Unit	
	Jennifer Dunston	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 May 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-48* is/are pending in the application.

4a) Of the above claim(s) *25-30 and 35-46* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-34,47 and 48* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

5.00

DETAILED ACTION

This action is in response to the Amendment, filed 5/31/2005, in which claims 1-24 were canceled; claims 25-30 and 35-46 were withdrawn; claims 31-34 were amended; and claims 47-48 were newly added. Applicants' arguments have been thoroughly reviewed, but are not persuasive for the reasons that follow. Any rejections and objections not reiterated in this action have been withdrawn. **This action is FINAL.**

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Election/Restrictions

Claims 25-30 and 35-46 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 12/29/2004.

This application contains claims drawn to an invention nonelected with traverse in an amendment filed 12/29/2004. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Currently, claims 31-34 and 47-48 are under consideration.

Claim Rejections - 35 USC § 101

Claims 31-34 and 47-48 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. **This rejection has been altered to address the amendments to the claims.**

When determining whether the utility of an invention has been described, one determines whether applicant has described a well-established utility. If not, it is determined whether applicant has made an assertion of specific and substantial utility. In contrast to general utility, a specific utility will be specific to the claimed subject matter. A substantial utility defines a real world utility of the invention, and utilities that require or constitute carrying out further research to identify or reasonably confirm a "real world' context use are not substantial utility (see utility guidelines, Federal Register January 5, 2001, Vol. 66, No. 5, pages 1092-1099).

Claims 31-34 and 47-48 are drawn to the amino acid sequence of Ghrelin Variant 2, a naturally occurring splice variant transcribed from the human Ghrelin locus. The protein is encoded by the nucleic acid sequence of SEQ ID NO: 11 and the amino acid sequence of the variant protein is described in SEQ ID NO: 32. Further, the claims are drawn to amino acid sequences having 90 % identity to the protein of SEQ ID NO: 32 and to amino acid sequences encoded by a nucleic acid with 90 % identity to SEQ ID NO: 11. Because a single nucleotide substitution can result in a missense mutation, a nucleic acid sequence with 90 % identity to nucleotides 112-462 of SEQ ID NO: 11 can encode a protein with less than 90% identity to the polypeptide of SEQ ID NO: 32. Moreover, the claims are drawn to peptides comprising at least 10 or 10-20 contiguous amino acids of the Ghrelin Variant 2 protein, wherein the contiguous

amino acid segment comprises at least one contiguous amino acid from amino acids 31-117 of SEQ ID NO: 32.

The disclosed utilities for the amino acid sequence of the instant invention are (i) the treatment of obesity and/or diabetes (e.g. pages 50-51), and (ii) the production of antibodies (e.g. page 52, lines 10-23). The specification asserts that the amino acid sequence of SEQ ID NO: 32 is encoded by SEQ ID NO: 11, which is an "obesity and/or diabetes nucleic acid sequence." While the specification asserts that the polypeptide of SEQ ID NO: 32 (i.e. Ghrelin Variant 2) can be used to treat diabetes and/or obesity, the relationship between Ghrelin Variant 2 and diabetes and/or obesity is not clearly described in the specification. The specification does not describe the relationship between the Ghrelin Variant 2 and any cognate receptor. Therefore, it is not clear whether the Ghrelin Variant 2 protein is intended to act as an agonist or antagonist of physiological pathways related to diabetes and/or obesity. Further, there is no art of record that discloses the function of the Ghrelin Variant 2 protein. Therefore, the asserted utility of the treatment of diabetes and/or obesity with the Ghrelin Variant 2 protein is not supported by a well established utility. Moreover, the asserted utility of treatment of obesity and/or diabetes is not substantial because the function and effects of the protein are not known. Further experimentation would be required to determine a "real world" context for the Ghrelin Variant 2 protein in the treatment of diabetes and/or obesity. Raising antibodies is not a specific utility because the asserted utility is not specific to Ghrelin Variant 2 in that any protein can be used to make an antibody. Further, the specification does not provide a substantial utility for the antibodies raised against Ghrelin Variant 2 protein or fragments thereof. Without knowing how the Ghrelin Variant 2 protein functions, one would not be able to predict the effect of

administering antibodies against Ghrelin Variant 2 protein to a patient with diabetes and/or obesity. Therefore, further experimentation would be required to determine a "real world" context for the antibodies against Ghrelin Variant 2 protein.

Thus, the asserted utilities for Ghrelin Variant 2 protein are not specific and substantial. The asserted utilities require carrying out further research to identify or reasonably confirm a "real world" context of use.

Claims 31-34 and 47-48 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

Response to Arguments--35 USC § 101

Applicant's arguments filed 5/31/2005 have been fully considered but they are not persuasive.

The response asserts that wild-type Ghrelin has a well-established utility as a stimulator of growth hormone secretion, as an orexigeneic molecule, as an adiopgenic molecule, as a protector of cardiac dysfunction, as a simulator of gastric acid secretion, as a stimulator of gastric motility, as a modulator of circulating glucose release, as an enhancer of insulin resistance, as a stimulator of gluconeogensis, and as an inducer of hunger sensations. This is not found persuasive because the claims are not drawn to wild type human Ghrelin. The claims are drawn to a Ghrelin variant 2 protein (SEQ ID NO: 32). A well-established utility is a specific,

substantial, and credible utility which is well known, immediately apparent, or implied by the specification's disclosure of the properties of a material, alone or taken with the knowledge of one skilled in the art. The sequence of the claimed variant differs from the prior art, wild-type Ghrelin protein. There is no evidence that the claimed protein has the same function as the wild-type Ghrelin. Therefore, the known functions of wild-type Ghrelin do not provide utility for the claimed Ghrelin variant 2 protein. The function of Ghrelin variant 2 may differ from the wild-type Ghrelin, and to confirm the function of the Ghrelin variant 2 protein, basic research would be required. Further research would be required to study the mechanisms involved in the function of Ghrelin variant 2 protein with regard to diabetes and/or obesity. Therefore, the wild-type Ghrelin protein function does not provide a well-established utility, or a specific and substantial utility for the claimed proteins.

The response asserts that wild-type Ghrelin peptide fragments as small as five amino acids (Gly-Ser-Ser(n-octanoyl)-Phe-Leu) have been shown to be agonists of the growth hormone secretagogue receptor 1a and to increase body weight in rats. The acylated prior art peptide differs from the claimed Ghrelin variant 2 sequences and is not encompassed by the claimed fragments of at least 10 amino acids. The claimed fragments must contain additional sequence relative to the prior art Ghrelin peptides. Further, the claims encompass fragments that do not contain any identity to wild-type Ghrelin. Further, the claims are not drawn to peptides with an n-octanoyl acylation of the serine residue. There is no evidence that the claimed proteins have the same function as the known or commercially available wild-type Ghrelin fragments. Therefore, the fragments of wild-type Ghrelin do not provide a well-established utility, or a specific and substantial utility for the claimed proteins.

For these reasons, the rejection is maintained.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 33 and 34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new matter rejection**.

Claims 33 and 34 are drawn to an isolated peptide comprising at least a 10 contiguous amino acid segment, or a 10-20 contiguous amino acid segment, of the isolated amino acid sequence of SEQ ID NO: 32, wherein the contiguous amino acid segment comprises at least one contiguous amino acid from amino acids 37-117 of SEQ ID NO: 32. The specification envisions fragments of 10 contiguous amino acid residues or at least 10-20 contiguous amino acid residues (e.g. paragraph bridging pages 49-50). The specification does not describe the sub-genus of fragments that are limited to a sequence comprising at least one contiguous amino acid from amino acids 37-117 of SEQ ID NO: 32.

Therefore, the specification does not provide support for the broad genus of protein fragments that comprise at least one contiguous amino acid from amino acids 37-117 of SEQ ID NO: 32.

Claims 33, 34, 47 and 48 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. **This is a new rejection necessitated by the amendment to the claims**.

The claims are drawn to peptides comprising at least a 10 contiguous amino acid segment, or a 10-20 contiguous amino acid segment, of the isolated amino acid sequence of SEQ ID NO: 32, wherein the contiguous amino acid segment comprises at least one contiguous amino acid from amino acids 37-117 of SEQ ID NO: 32. Further, the claims are drawn to a set of amino acid sequences with 90% identity to the amino acid sequence of the protein encoded by nucleotides 112-462 of SEQ ID NO: 11 (i.e. SEQ ID NO: 32). Further, the claims are drawn to a set of amino acid sequences encoded by a nucleotide sequence having 90% identity to nucleotides 112-462 of SEQ ID NO: 11. These amino acid sequences may have much less than 90% identity to the sequence of SEQ ID NO: 32, because a single point mutation in the nucleic acid can create a missense mutation. The rejected claims thus comprise a set of proteins and fragments defined by percent identity.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of a complete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, and any combination thereof. The specification describes the amino acid sequence encoded by bases

112-462 of SEQ ID NO: 11. Bases 112-462 of SEQ ID NO: 11 encode the protein of SEQ ID NO: 32. The protein of SEQ ID NO: 32 is described as a naturally occurring sequence resulting from alternative splicing of Ghrelin (e.g. page 4, lines 4-13). The specification broadly envisions conservative substitutions, non-conservative substitutions and fragments of the protein (e.g. paragraph bridging pages 49-50). The description of the full-length sequence of SEQ ID NO: 32, for which the specification does not teach a function or activity, is not representative of the broad genus of mutants, variants, homologs and polypeptides comprising a sequence that is less than an identical to the full-length sequence of SEQ ID NO: 32. Since the specification has not taught the function or biological activity of SEQ ID NO: 32, or the functional domains of the protein, one could not envision changes that would result in a functional protein.

The prior art does not appear to offset the deficiencies of the instant specification in that it does not describe the function of the protein of SEQ ID NO: 32 and does not provide a structure-function correlation for one to envision variants defined by percent identity or fragments comprising at least one amino acid from amino acids 37-117 of SEQ ID NO: 32. The prior art does teach functional fragments with 100% identity to amino acids 1-36 of SEQ ID NO: 32 (Sheppard et al, US Patent No. 6,291,653, cited in a prior action; e.g. SEQ ID NO: 2). The prior art teaches that fragments consisting of the amino acid sequence GSSFLSPEHQ, GSSFL, and GSSF, wherein the second serine residue is acylated with an n-octanoyl group, have functional activity in an assay for GHSR1a activation (Bednarek et al. J. Med. Chem. Vol. 43, pages 4370-7376, 2000; e.g. Table 4; page 4376, Aequorin Bioluminscence Functional Assay). However, the claimed fragments cannot consist of this known sequence and must contain

additional sequence that differs from the prior art sequence. The prior art or instant specification does not describe any functional sequences within amino acids 37-117.

Given the very large genus of fragments and variants defined by percent identity encompassed by the rejected claims, and given the limited description provided by the prior art and specification with regard to the function of the protein of SEQ ID NO: 32 and the functional domains of SEQ ID NO: 32, the skilled artisan would not have been able to envision a sufficient number of specific embodiments that meet the functional limitations of the claims to describe the broadly claimed genus of proteins. Thus, there is no structural/functional basis provided by the prior art or instant specification for one of skill in the art to envision those modifications that satisfy the limitations of the claims. Therefore, the skilled artisan would have reasonably concluded applicants were not in possession of the claimed invention for claims 33, 34, 47 and 48.

Conclusion

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period

will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jennifer Dunston whose telephone number is 571-272-2916. The examiner can normally be reached on M-F, 9 am to 5 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Remy Yucel can be reached at 571-272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR, http://pair-direct.uspto.gov) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Jennifer Dunston
Examiner
Art Unit 1636

jad

TERRY MCKELVEY
PRIMARY EXAMINER